RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1, 2, 4-8, 10-16, and 18-31 are currently pending. Claim 31 has been amended. Claims 15, 16, and 18-29 have been withdrawn. Claims 3, 9, and 17 have been canceled.

Support for the amendment to claim 31 appears at least at page 22, ¶0041, of the specification as filed. Support for new claims 32-35 appears at least at page 7, ¶0019, of the application as filed.

No new matter has been added by way of this Response.

B. Rejection Under 35 U.S.C. §103

The Action rejects claims 1-2, 4-8, 10-14, and 30 as obvious over Frame *et al.*, *Plant Physiology*, 2002, vol. 129, pages 13-22 ("Frame") in view of Zhao *et al.*, *Molecular Breeding*, vol. 8, pages 323-222 ("Zhao") and further in view of U.S. Patent No. 6,329,571, issued to Hiei *et al.* ("Hiei").

According to the Action, Frame and Zhao teach transformation of cereals. The Action admits that neither Frame nor Zhao teaches selection at between about 30°C and about 34°C. However, the Action relies on Hiei to teach this element. Thus, the Action finds it would be *prima facie* obvious to combine the references to arrive at the invention. Applicants respectfully traverse.

The Action relied on column 7, lines 31-49 of Hiei for its alleged teachings. However, this relied upon portion relates to selection temperature for rice, not maize. Nowhere does Hiei teaches a selection temperature for maize. Rice and maize have different genetic architecture and physiological mechanism, and thus behave differently to environmental influences such that

there would be no expectation of success with respect to maize. For example, rice genome size ranges between 415 and 460 Mb but maize genome size ranges between 2,300 and 2700 Mb. Rice is a C3 plant but maize is a C4 plant. Rice does not grow well in low temperatures, but maize grows well in relatively low temperatures. Accordingly, rice and maize respond differently. Therefore, a selection temperature for rice does not teach or suggest anything for determining an optimal selection temperature for maize.

The Action of December 11, 2007 (incorporated by reference into the present Action as the basis for rejection), at page 3, states that "[g]iven the state of the prior art showing the differences of selection temperatures used for various explants, organisms...undue experimentation would be required to determine the effect of increased selection temperature on the transformation efficiency for any organism." Thus, the Action acknowledges that a selection temperature for a given organism is unpredictable because extensive research is required to identify the conditions effective for each specific organism. This is because plant species are sufficiently diverse that each species may respond differently and exhibit different sensitivity to different temperatures. Accordingly, one of skill in the art would not expect any success for maize selection temperature based on Hiei's teachings on rice.

The Action of December 11, 2007 (which is the basis of the present rejection), at page 3, also states that "the effect of increased temperature during selection on the transformation efficiency for various transformation methods using various explants are not well known in the art." Thus, Applicants note that the Action also acknowledges that the cited art is lacking any suggestion or motivation to select transformed cells at higher temperature range defined by the present claims. In fact, at the time of filing the current application, selection temperature was not

regarded as an important parameter for investigation in studies of transformation efficiency. There is therefore no basis for the obviousness rejection.

In a determination of obviousness, the proper question is whether one of ordinary skill in the art would have seen an obvious benefit to upgrading conventional selection techniques so as to reach the requirements of the present claims (*see KSR Int'l Co.*, at 6). The mere fact that references *can* be combined or modified does not render the resultant combination obvious unless there is some reason that *suggests the desirability* of the combination. MPEP §2143.01(III). The Office has failed to make such a showing. Nothing in the cited art suggests any benefit could be obtained by increasing selection temperatures or in particular by use of selection at 30°C or higher in maize. Specifically, nothing in the cited prior art suggests any desirability of use of selection at 30°C or higher in maize. For example, Hiei indicates nothing of any benefit of using a 30°C selection in rice or even of any difference at all *vis a vis* any other temperature. It is therefore pure hindsight to suggest that one of skill in the art would have sought to apply this temperature to another crop or to try to modify the temperature parameter in any way.

Selection temperature was not a parameter that would routinely be varied at the time of filing, absent the present disclosure. In contrast, Applicants have shown that such conditions can be used to achieve increased transformation frequency, as seen in Example 8 and Table 3 of the specification. Accordingly, one of skill in the art would have been without reasonable expectation at the time of filing of the present application that increasing the selection temperature would increase transformation frequency, and would be without any reason to attempt to modify any prior selection temperature criteria.

Moreover, the increase in transformation frequency upon selection at higher temperatures is conceded to be unexpected. In particular, the previous Action states "[i]t may be true that the increase in transformation frequency upon selection at high temperature is unexpected...." *See* Action dated June 27, 2007, page 6. Applicants respectfully submit that the invention can not simultaneously be both obvious and unexpected.

In sum, neither Frame nor Zhao is asserted to teach the claimed selection temperature discussed above, and thus neither Frame nor Zhao cures the defects in Hiei. The Action has failed to establish any benefit to upgrading conventional maize selection techniques and failed to show any desirability of modifying or combining the references to reach the requirements of the claims, particularly the use of selection at 30°C or higher in maize. The rejection is therefore believed moot and removal thereof is respectfully requested.

1. Claim 31

Furthermore, additional claims recite further patentable features of the invention that are not addressed by the reasoning of the Action. For example, claim 31 recites, "culturing the transformed maize tissue at a first temperature for a first period of time and at a second temperature for a second period of time...wherein the first temperature ranges from about 30°C to about 34°C and the second temperature is about 27°C." Accordingly, claim 31 requires a dual selection temperature regime for selection of transformed tissues. Example 8, Table 3 of the specification shows that the claimed dual selection temperature regime yielded transformation frequency ranging from 6.7% to 8.4%. As discussed above, the cited references do not teach selection temperature for maize, and thus, one of skill in the art would have been without reasonable expectation at the time of filing of the patent application that the claimed dual selection temperature would yield transformation frequency ranging from 6.7% to 8.4% in

maize. Accordingly, the results were unpredictable and unexpected in light of the cited references.

The Final Action nonetheless asserts that the dual selection temperatures recited in claim 31 are indistinguishable from the selection method at 28°C as taught by Frame in view of Zhao, and that prolonged selection time is regarded as optimization of process parameters and would not confer a patentable distinction. But a particular parameter must first be recognized as a result-effective variable, *i.e.*, a variable which achieves a *recognized result*, before the determination of the optimum or workable ranges of said variable might be characterized as routine. *See* MPEP §2144.05(II)(B). None of the cited references even recognize the benefit or effect generally of selection at higher temperatures, and so, could not teach or suggest optimization of such variable (*see* MPEP §2144.05(II)(B), requiring recognition of a result-effective variable before optimization is routine). As such, one of ordinary skill in the art would have no reason and expect no benefit in optimizing selection time and/or temperature because there was no recognition at the time of filing that such variables impacted transformation efficiency.

2. Unexpected Results Conferred by the Invention

In refuting Applicants' arguments of unexpected results in the previous Response, the Final Action improperly challenges the experimental design and statistical validity of presented conclusions of the specification, particularly Example 8, without providing any (required) evidentiary showing in support of such challenges.

Assertions of technical facts in the areas of specific knowledge of the prior art must *always* be supported by citation to some reference work recognized as standard in the pertinent art. MPEP § 2144.03(A). Official notice unsupported by documentary evidence should only be

taken in an Action where the facts asserted to be well-known, or to be common knowledge in the art are capable of instant and unquestionable demonstration as being well-known. MPEP § 2144.03(A). Under MPEP §2164.04, unless there is a reason to doubt the objective truth of statements contained in the specification disclosure, such subject matter must be accepted as a description supporting the claimed invention. Where an Action "doubts the truth or accuracy of any statement in a supporting disclosure" it must "back up assertions [in the Action] with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).

The Final Action in particular asserts that increased transformation efficiency upon selection at higher temperatures is not unexpected because "out of 5 experimentations, only two of them show an increase in transformation frequency" (Action, p. 4, ln. 13-18). However, the Final Action overlooks the fact that each experiment consisted of hundreds of explants and that the statistically valid conclusions presented in Example 8, Table 3, were supported by at least 1500 explants in each of four treatments, across five experiments. In addition to the results presented in Table 3, Example 8 describes further experiments (*i.e.*, in addition to those of Table 3) that compared 27°C with 30°C, with results as follows:

> A direct comparison of the two temperatures during the same experiment had a transformation frequency of 3.4% for 27°C and 9.9% for 30°C. Over a large number of transformations at 27°C, transformation frequency averaged 5.5%. At 30°C, transformation frequency averaged 15%. Overall, the increase in temperature during selection increased the transformation frequency by about twofold.

As shown above, the results of Example 8 clearly demonstrate increased transformation efficiency upon selection at higher temperatures. Neither the Final Action nor the cited references provide any reason to expect such an increased transformation efficiency. The Final Action has failed to provide any citation to support its challenges to the experimental design and statistical conclusions of Example 8. The Final Action has also failed to show that one of ordinary skill in the art would instantly and unquestionably accept the Final Action's unsupported challenges to the experimental design and statistical conclusions of Example 8, and fails to provide any acceptable evidence or reasoning to back up assertions challenging the truth and/or accuracy of statements contained in Example 8. As such, there is insufficient reason provided to doubt that the specification provides unexpected results of increased transformation efficiency upon selection at higher temperatures.

The Final Action further asserts that "experiment 4921 is a failure and should be excluded from the calculation [of transformation frequency]." The Final Action provides no citation or reasoning in support of its technical assertions regarding how the experimental design and statistics of Example 8 ought to have been conducted. The present specification provides that major deficiencies of current plant transformation systems include production efficiency and transformation variability. Contrary to the Final Action's assertions, experimental results with regard to selection at 27°C presented in Example 8 (*see e.g.*, Table 3) are not "failures", but rather, effective demonstrations of the very deficiencies sought to be overcome through various aspects of the present invention.

Thus, contrary to its administrative burden otherwise, the Final Action fails to support the assertion that the experimental design, data, and conclusions of the specification are questionable. In the absence of such showing, it should be accepted that the specification

describes unexpected increases in transformation frequency from increased selection temperature.

In view of the foregoing, withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants respectfully request favorable consideration of this case.

The Examiner is invited to contact the undersigned attorney at (214) 259-0931 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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